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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/530,363	05/01/00	GABERT J	1721-21

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EXAMINER	
SPIEGLER, A	
ART UNIT	**PAPER NUMBER**
1656	9

DATE MAILED: 09/25/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/530,363	GABERT, JEAN	
	Examiner	Art Unit	
	Alexander H. Spiegler	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. This action is in response to Paper No. 7, filed on July 10th, 2001. Currently, claims 16-38 are pending. All arguments have been full considered and thoroughly reviewed, but are deemed not persuasive for the reasons which follow. This action is made FINAL. Any objections and rejections not reiterated below are hereby withdrawn.

Specification

2. The specification should be amended to insert the appropriate sequence identifying (SEQ ID NO) following each recited sequence (see pages 21-23).

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 16-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 16-38 are indefinite over the recitation of "a step of anchored PCR" because it is not clear as to what step is actually performed.

B) Claims 16-38 are indefinite over the recitation of "a step of anchored PCR" because the claims do not recite an actual process step of anchored PCR in the body of the claims. (i.e. the preamble states a step of anchored PCR, whereas the claims refer to amplification of DNA by asymmetrical PCR).

C) Claims 16-38 are indefinite over the recitation of "complementary random primer" because it is not clear as to what is meant by this recitation. This recitation is not an art recognized term, and furthermore, this recitation is not defined in the specification.

D) Claims 16-38 are indefinite over the recitation of "all the gene rearrangements" because it is not clear as to how one can determine "all the gene rearrangements" by simply performing one or more asymmetrical amplification reactions.

E) Claims 16-38 are indefinite over the recitation of "the gene rearrangements" because this recitation lacks antecedent basis.

F) Claims 16-38 are indefinite over the recitation of "any part of the genome adjacent to the target gene" because it is not clear as to what is meant by this recitation. It is not clear as to how one determines "any part of the genome adjacent to the target gene". (i.e. the metes and bounds of the claims are indefinite).

G) Claims 16-38 are indefinite over the recitation of "when present" because it is not clear as to what this recitation refers to.

H) Claims 32-38 are indefinite over the recitation of "reagents for carrying out the PCR and the detection step" because it is not clear as to what reagents are needed "for carrying out the PCR and the detection step".

I) Claims 33 is indefinite due to the improper expression of alternative limitations (i.e. the recitation of "selected in the group consisting of"). "Alternative expressions are permitted if they present no uncertainly or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a

Markush group, recites members as being 'selected from the group consisting of A, B, and C'." (MPEP 2173.05(d).

J) Claim 33 is indefinite over the recitation of "random partners" because it is not clear as to what this is referring to.

K) Claim 33 is indefinite over the recitation of "the gene" because this recitation lacks antecedent basis.

L) Claim 34-38 is indefinite over the recitation of "the polypeptidic nucleic acids" and "the ribozymes" for lack of antecedent basis.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 16-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Corral et al. (PNAS (1993) 90: 8538-42), in view of Liu et al. (Genomics (1995) 25: 674-681).

Corral teaches acute leukemias of different linkages having similar MLL gene fusions encoding related chimeric proteins resulting from chromosomal translocations. Specifically, the reference teaches the MLL gene undergoes chromosomal translocation in acute leukemia resulting in gene fusion with AF4 and ENL (see abstract). Furthermore, the reference teaches that the breakpoints of these translocations create this fusion of the MLL gene and the AF4 gene (pg. 8538). The reference also teaches the use of a primer EX5NP (exon 5) in a reverse-anchored-PCR reaction (pg. 8539). The reference further teaches the use of probes in the

detection of rearrangements (pg. 8539). The reference does not teach a pair of primers, wherein one primer is a sequence-specific primer and the other primer is a random primer.

Liu teaches the method of thermal asymmetric interlaced PCR. Specifically, Liu teaches the method of asymmetric PCR using a single pair of primers, wherein one primer is a sequence-specific primer and the other primer is a random primer (see abstract). The reference also teaches the detection of the PCR products (pg. 675) and the use of specific probes in genome mapping and map-based cloning programs (pg. 674). Furthermore, the reference teaches that this method is beneficial over other methods for several reasons (i.e. higher specificity, higher efficiency, speed, etc.) (pgs. 679-680).

One of ordinary skill in the art would have been motivated to use the method of Corral to detect gene rearrangements using an anchored PCR method comprising a pair of primers, wherein one primer is a sequence-specific primer, and the other primer is a random primer, to provide a more specific and efficient method of detection. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Corral of detecting gene rearrangements associated with the MLL gene, by using a pair of primers, wherein one primer is a sequence-specific primer and the other primer is a random primer, to provide a more effective method of detection. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have further modified the methods of Corral and Liu, by using molecular biology assays that are well known and of common knowledge in the art, such as, using a label for detection purposes, antibody-enzyme detection, and the use of solid supports. Furthermore, with respect to claims 32-38, reagent kits for performing DNA detection assays were conventional in the field of molecular

biology at the time the invention was made. In particular, kits provide the advantage of pre-assembling the specific reagents required to perform an assay and ensure the quality and compatability of the reagents to be used in the assay. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged an agent capable of cleaving a gene (i.e. restriction enzyme), and a probe with a 5'biotin group attached therein, wherein said probe is bonded to a DNA chip, in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art.

In the response of Paper No. 7, Applicant traverses the obviousness rejection of Corral et al. (PNAS (1993) 90: 8538-42), in view of Liu et al. (Genomics (1995) 25: 674-681). Applicant argues that "the translocations of Corral are analyzed by Southern blots on patient's genomic DNA or by PCR (or RAP) and sequencing...and that Southern blots would not have enabled two fragments of the same size to be discriminated and the combination PCR/sequencing is totally inappropriate for a commercial diagnostic test due to the labor-intensive nature of the operation" (page 15 of the response). Applicant further argues that there is no teaching or suggestion in Corral or Liu to amplify all target genes and only detect those which have undertaken a rearrangement using the probes as defined in the present invention.

Applicants arguments have been considered, but are not persuasive for the following reasons. First, applicants are arguing limitations that are not found in the claims. The claims do not require that "two fragments of the same size are to be discriminated". The claims simply require that PCR products with rearranged genes are to be detected, and makes no mention of any size requirements or limitations in the detection of fragments of the same size. Applicant's argument regarding the "inappropriateness" of a PCR/sequencing for a commercial diagnostic

test, due to the labor-intensive nature of the operation, is considered not to be not pertinent with respect to the discussion of the claims. Applicant further argues that there is no teaching or suggestion in Corral or Liu to amplify all target genes and only detect those which have undertaken a rearrangement using the probes as defined in the present invention. This argument is not persuasive, since the claims do not require the amplification of "all target genes". Furthermore, it is not clear as to how the present invention would amplify "all target genes" when only one asymmetrical PCR is required. Also, it is not clear as to how one detects those genes which have "undertaken a rearrangement using the probes of the present invention".

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alexander H. Spiegler
September 24, 2001

KENNETH R. HORLICK
PRIMARY EXAMINER
GROUP 1600

9/24/01